

(FILE 'HOME' ENTERED AT 18:01:40 ON 21 MAR 2003)

FILE 'USPATFULL, CAPLUS, AGRICOLA, ALUMINIUM, ANABSTR, APOLLIT, AQUIRE, BABS, BIOCOMMERCE, BIOTECHNO, CABA, CAOLD, CBNB, CEABA-VTB, CEN, CERAB, CIN, COMPENDEX, CONFSCI, COPPERLIT, CORROSION, ENCOMPLIT, ENCOMPLIT2, FEDRIP, GENBANK, INSPEC, INSPHYS, INVESTEXT, ..' ENTERED AT 18:02:16 ON 21 MAR 2003

L1	41069 S ADA
L2	59 S L1 AND SIRS
L3	1 S L2 AND COFORMYCIN
L4	0 S COFORMYCIN AND INHIBITION OF ADENINOSINE DEAMINASE
L5	394 S COFORMYCIN AND ADENOSINE DEAMINASE
L6	41 S L5 AND PENTOSTATIN
L7	0 S L6 AND SIRS
L8	54 S ADENOSINE DEAMINASE AND ADENOSINE MONOPHOSPHATE DEAMINASE

L3 ANSWER 1 OF 1 USPATFULL  
 AN 1998:31136 USPATFULL  
 TI Inhibitors of adenosine monophosphate deaminase  
 IN Erion, Mark D., Del Mar, CA, United States  
 Bookser, Brett C., Solana Beach, CA, United States  
 Kasibhatla, Srinivas Rao, San Diego, CA, United States  
 Gruber, Harry E., Rancho Santa Fe, CA, United States  
 PA Gensia Sicor Inc., San Diego, CA, United States (U.S. corporation)  
 PI US 5731432 19980324  
 AI US 1994-192154 19940203 (8)  
 RLI Continuation-in-part of Ser. No. US 1993-12841, filed on 3 Feb 1993  
 DT Utility  
 FS Granted  
 LN.CNT 2952  
 INCL INCLM: 540/568.000  
 INCLS: 514/221.000; 540/554.000  
 NCL NCLM: 540/568.000  
 NCLS: 540/554.000  
 IC [6]  
 ICM: C07D491-04  
 EXF 540/554; 540/568; 514/221  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d L3 1 std, kwic

L3 ANSWER 1 OF 1 USPATFULL  
 AN 1998:31136 USPATFULL  
 TI Inhibitors of adenosine monophosphate deaminase  
 IN Erion, Mark D., Del Mar, CA, United States  
 Bookser, Brett C., Solana Beach, CA, United States  
 Kasibhatla, Srinivas Rao, San Diego, CA, United States  
 Gruber, Harry E., Rancho Santa Fe, CA, United States  
 PA Gensia Sicor Inc., San Diego, CA, United States (U.S. corporation)  
 PI US 5731432 19980324  
 AI US 1994-192154 19940203 (8)  
 RLI Continuation-in-part of Ser. No. US 1993-12841, filed on 3 Feb 1993  
 DT Utility  
 FS Granted  
 LN.CNT 2952  
 INCL INCLM: 540/568.000  
 INCLS: 514/221.000; 540/554.000  
 NCL NCLM: 540/568.000  
 NCLS: 540/554.000  
 IC [6]  
 ICM: C07D491-04  
 EXF 540/554; 540/568; 514/221  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . metabolized either via phosphorylation of the 5'-hydroxyl by adenosine kinase ("AK") to give AMP or via deamination by adenosine deaminase ("ADA") to give inosine. Factors that determine the predominate pathway include local adenosine concentrations, kinetic characteristics of ADA and AK, and ADA versus AK intracellular specific activity. Since physiological adenosine concentrations are <100 nM and since ADA has a 100-fold higher Km for adenosine (Km=.about.50 µM) relative to that of AK (Km=0.5 µM), ADA may be a significant factor in adenosine metabolism only at high adenosine concentrations. The rapid breakdown of ATP during ischemia leads to elevated local adenosine levels. Consequently, if adenosine levels are raised 100 fold during ischemia, ADA may begin to become important in local adenosine metabolism.

SUMM Chronic total inhibition of ADA has been reported to lead to severe immunodeficiency. Children that are genetically deficient in

**ADA** lack T- and B-cell activity and therefore are prone to a wide variety of life-threatening infections and diseases. Irreversible inhibition of **ADA** by the potent inhibitor, 2'-deoxycoformycin, has been reported to lead to a loss in B- and T-cell function and overall immunodeficiency. Although **ADA** deficiency and **ADA** inhibition leads to immunodeficiency, these studies have not found higher plasma adenosine levels.

SUMM Four **coformycin** analogs have been reported to show activity as AMPDA inhibitors. The 5'-phosphorylated analogs of **coformycin** and deoxycoformycin have been reported to be potent inhibitors of rabbit muscle AMPDA ( $\leq 1$  nM). These compounds, however, are not. . . . vivo, which is a common and rapid metabolic pathway for other 5'-monophosphate nucleotides and other organophosphates in general would produce **coformycin** and deoxycoformycin respectively. **Coformycin** and deoxycoformycin are very potent inhibitors of **ADA** ( $< 0.2$  nM) but are significantly weaker AMPDA inhibitors (1000 nM). Kinetic studies on the inhibition of **ADA** with **coformycin** and deoxycoformycin have shown that these compounds are tight binding inhibitors that result in irreversible inhibition of **ADA**. Consequently, inhibition of AMPDA with these compounds would lead to complete inhibition of **ADA**.

SUMM Other **coformycin** analogs that have been reported include the aglycon attached to a short oxygenated chain, (acyclocoformycin in Showalter, et al., J. . . .

SUMM . . . . syndrome. Further, the compounds of the present invention are especially useful in the treatment or prevention of septic shock, sepsis, **SIRS** (**SIRS** is defined in Critical Care Medicine, vol 20, page 864-874, 1992, as a condition with no other apparent cause characterized. . . .

SUMM The term "**coformycin** aglycone" refers to 3',6',7',8'-tetrahydroimidazo [4',5'-d] [1',3']diazepin-8-ol.

SUMM 3-(trans-3',7'-dimethyl-2',6'-octadienyl)**coformycin** aglycone,

SUMM (3'R)-3-(3',7'-dimethyloct-6'-enyl)**coformycin** aglycone,

SUMM (1'S,2'S,5'S)-3-(6',6'-dimethyl[3,1,1]-bicyclohept-2'-methyl)**coformycin** aglycone (compound 1e),

SUMM (1'R,2"S,5"R)-3-(2'-(2"-isopropyl-5"-methylcyclohexyloxy)ethyl)**coformycin** aglycone,

SUMM 3-(naphth-2'-ylmethyl)**coformycin** aglycone,

SUMM 3-(2'-(naphth-1"-yl)ethyl)**coformycin** aglycone,

SUMM 3-(2'-(naphth-2"-yl)ethyl)**coformycin** aglycone,

SUMM 3-(2'-phenylethyl)**coformycin** aglycone,

SUMM 3-(2'-(2"-methylphenyl)ethyl)**coformycin** aglycone,

SUMM 3-(6'-carboxyhexyl)**coformycin** aglycone,

SUMM 3-(7'-carboxyheptyl)**coformycin** aglycone,

SUMM 2-amino-3-(5'-carboxy-5'-carbobenzyloxypropyl)**coformycin** aglycone,

SUMM 2-bromo-3-(5'-carboxy-5'-carbobenzyloxypropyl)**coformycin** aglycone,

SUMM 3-(5'-carbox-N-(4"-chlorobenzyl)amido-5'-carboxypropyl)**coformycin** aglycone,

SUMM 3-(5'-carboxamido-5'-carboxyhexyl)**coformycin** aglycone,

SUMM 3-(2'-(o-carboxyphenylthio)ethyl)**coformycin** aglycone,

SUMM 3-(3'-(3"-carboxy-6"-methylphenyl)propyl)**coformycin** aglycone,

SUMM 3-(3'-(2"-methoxy-5"-carboxyphenyl)propyl)**coformycin** aglycone,

SUMM 3-(3"-carboxy-6"-propylphenyl)ethyl)**coformycin** aglycone,

SUMM 3-(3"-carboxy-6"-hydroxymethylphenyl)ethyl)**coformycin** aglycone,

SUMM 3-(2'-(3"-carboxyphenyl)ethyl)**coformycin** aglycone,

SUMM 3-(3'-(2"-carboxy-3"-fluorophenyl)propyl)**coformycin** aglycone,

SUMM 3-(3'-(2"-carboxythiophen-3"-yl)propyl)**coformycin** aglycone,

SUMM 3-(2'-(2"-carboxythiophen-5"-yl)ethyl)**coformycin** aglycone,

SUMM 3-(3'-(2"-carboxynaphthyl)propyl)**coformycin** aglycone,

SUMM 2-bromo-3-(2'-3"-carboxynaphthyl)ethyl)**coformycin** aglycone,

SUMM 2-amino-3-(2'-carboxynaphthyl)ethyl)**coformycin** aglycone,

SUMM 2-amino-3-(2'-(3"-bromo-5"-carboxyphenyl)ethyl) **coformycin**  
aglycone,

SUMM 2-bromo-3-(2'-3"-bromo-5"-carboxyphenyl)ethyl) **coformycin**  
aglycone,

SUMM 2-bromo-3-(5'-carboxy-6'-(3"-bromophenyl)hexyl) **coformycin**  
aglycone,

SUMM 2-amino-3-(5'-carboxy-6'-(3"-bromophenyl)hexyl) **coformycin**  
aglycone,

SUMM 3-[2'-(7"-carboxybenzopyran-5"-yl)ethyl] **coformycin** aglycone,

SUMM 3-[2'-(6"-carboxybenzopyran-8"-yl)ethyl] **coformycin** aglycone,

SUMM 3-[2'-(3"-carboxy-5",6",7",8"-tetrahydronaphthyl) ethyl]  
**coformycin** aglycone,

SUMM 3-[2'-(3"-carboxy-5",7"-benzodioxolyl)ethyl] **coformycin**  
aglycone,

SUMM 3-[2'-(6"-carboxy-2",3"-dihydrobenzofuran-4"-yl )ethyl] -  
**coformycin** aglycone,

SUMM 3-[2'-3"-carboxyindane)ethyl] **coformycin** aglycone,

SUMM 3-[2'-5"-carboxy-2",3"-dihydrobenzofuran-7"-yl )ethyl] -  
**coformycin** aglycone,

SUMM 3-[2'-(6"-carboxybenzothiophen-4"-yl)ethyl] **coformycin**  
aglycone,

SUMM 3-[2'-(6"-carboxybenzofuran-4"-yl)ethyl] **coformycin** aglycone,

SUMM 3-[2-(3"-carboxyanthracenyl)ethyl] **coformycin** aglycone,

SUMM 3-[2'-(3"-carboxyacenaphthylene)ethyl] **coformycin** aglycone,

SUMM 3-[2'-(3"-carboxyphenanthrenyl)ethyl] **coformycin** aglycone,

SUMM 3-(6'-carboxy-6'-carbobenzyloxyhexyl) **coformycin** aglycone,

SUMM 3-(5'-carboxy-6'-carbobenzyloxyhexyl) **coformycin** aglycone,

SUMM 3-(5'-carboxy-5',5'-dibenzylpentyl) **coformycin** aglycone,

SUMM 3-(5'-carboxy-5'-fluoro-6'-phenylhexyl) **coformycin** aglycone,

SUMM 3-(5'-carboxy-6'-(2"-chlorophenyl)hexyl) **coformycin** aglycone,

SUMM 3-(5'-carboxy-6'-(2"-iodophenyl)hexyl) **coformycin** aglycone,

SUMM 3-(5'-carboxy-6'-(2"-tolyl)hexyl) **coformycin** aglycone

SUMM 3-(5'-carboxy-6'-(2"-trifluoromethylphenyl)hexyl) **coformycin**  
aglycone,

SUMM 3-(5'-carboxy-6'-(2"-ethoxyphenyl)hexyl) **coformycin** aglycone,

SUMM 3-(5'-carboxy-6'-(2"-benzyloxyphenyl)hexyl) **coformycin**  
aglycone,

SUMM 3-(5'-carboxy-6'-(2"-hydroxyphenyl)hexyl) **coformycin** aglycone,

SUMM 3-(5'-carboxy-6'-(4"-fluorophenyl)hexyl) **coformycin** aglycone,

SUMM 3-(5'-carboxy-5'-(4"-fluorophenoxy)pentyl) **coformycin** aglycone,

SUMM 3-(5'-carboxy-5'-hydroxy-6'-phenylhexyl) **coformycin** aglycone,

SUMM 3-(5'-carboxy-5'-phenoxy)pentyl) **coformycin** aglycone,

SUMM 3-(5'-carboxy-5'-(4"-chlorophenoxy)pentyl) **coformycin** aglycone,

SUMM 3-(5'-carboxy-5'-benzyloxy)pentyl) **coformycin** aglycone,

SUMM 3-(5'-carboxy-5'-(4"-chlorobenzyloxy)pentyl) **coformycin**  
aglycone,

SUMM 3-(5'-carboxy-5'-(3"-bromophenoxy)pentyl) **coformycin** aglycone,

SUMM 3-(3'-(2"-bromo-4"-propoxyphenyl)propyl) **coformycin** aglycone,

SUMM 3-(3'-(2"-chloro-4"-propoxyphenyl)propyl) **coformycin** aglycone,

SUMM 3-[2'-(3"-Carboxy-6",8"-dichloronaphthyl)ethyl] **coformycin**  
aglycone,

SUMM 3-[2'-(3"-Carboxy-6",8"-difluoronaphthyl)ethyl] **coformycin**  
aglycone,

SUMM 3-[2'-(3"-Carboxy-6",8"-ditrifluoromethylnaphthyl) ethyl]  
**coformycin** aglycone,

SUMM 3-[2'-(3"-Carboxy-8"-chloronaphthyl)ethyl] **coformycin** aglycone,

SUMM 3-[2'-(3"-Carboxy-8"-trifluoromethylnaphthyl)ethyl] **coformycin**  
aglycone,

SUMM 3-[2'-(3"-Carboxy-8"-methylnaphthyl)ethyl] **coformycin** aglycone,

SUMM 3-[2'-(3"-Carboxy-8"-fluoronaphthyl)ethyl] **coformycin** aglycone,

SUMM 3-[2'-(3"-Carboxy-7"-chloronaphthyl)ethyl] **coformycin** aglycone,

SUMM 3-[2'-(3"-Carboxy-7"-bromonaphthyl)ethyl] **coformycin** aglycone,

SUMM 3-[2'-(3"-Carboxy-7"-trifluoromethylnaphthyl)ethyl] **coformycin**  
aglycone,

SUMM 3-[2'-(3"-Carboxy-7"-methylnaphthyl)ethyl] **coformycin**  
aglycone,

SUMM 3-[2'-(3"-Carboxy-7"-fluoronaphthyl)ethyl] **coformycin**  
aglycone,

SUMM 3-[2'-(3"-Carboxy-7"-phenoxynaphthyl)ethyl] **coformycin**  
aglycone,

SUMM 3-[2'-(3"-Carboxy-7"-phenylnaphthyl)ethyl] **coformycin** aglycone,

SUMM 3-[2'-(3"-Carboxy-7"-ethylnaphthyl)ethyl] **coformycin** aglycone,

SUMM 3-[2'-(3"-Carboxy-5"- (p-chlorophenoxy) naphthyl)ethyl] **coformycin**  
aglycone,

SUMM 3-[2'-(3"-Carboxy-5"-phenoxynaphthyl)ethyl] **coformycin**  
aglycone,

SUMM 3-[2'-(3-Carboxy-5",6",7"-trifluoronaphthyl)ethyl] **coformycin**  
aglycone,

SUMM 3-[2'-(3"-Carboxy-5",6"-difluoronaphthyl)ethyl] **coformycin**  
aglycone,

SUMM 3-[2'-(3"-Carboxy-5",7"-difluoronaphthyl)ethyl] **coformycin**  
aglycone,

SUMM 3-[2'-(3"-Carboxy-6"-bromo-7"-fluoromethylnaphthyl) ethyl]  
**coformycin** aglycone,

SUMM 3-[2'-(3"-Carboxy-9"-methoxyphenanthrene)ethyl] **coformycin**  
aglycone and

SUMM 3-[2'-(2"-Carboxy-4"-phenanthrene)ethyl] **coformycin** aglycone.

SUMM 3-(4'-benzylcycloheptyl) **coformycin** aglycone,

SUMM 3-(4'-(2"-phenylethyl)cycloheptyl) **coformycin** aglycone,

SUMM 3-(3'-benzylcycloheptyl) **coformycin** aglycone,

SUMM 3-(3'-(2"-phenylethyl)cycloheptyl) **coformycin** aglycone,

SUMM 3-(3'-cyclohexylpropyl) **coformycin** aglycone,

SUMM 3-2'-(2"-ethoxynaphth-1"-yl)ethyl) **coformycin** aglycone,

SUMM 3-2'-(3"-ethoxynaphth-1"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(4"-ethoxynaphth-1"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(5"-ethoxynaphth-1"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(6"-ethoxynaphth-1"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(7"-ethoxynaphth-1"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(8"-ethoxynaphth-1"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(naphth-2"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(1"-ethoxynaphth-2"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(3"-ethoxynaphth-2"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(4"-ethoxynaphth-2"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(5"-ethoxynaphth-2"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(6"-ethoxynaphth-2"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(7"-ethoxynaphth-2"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(8"-ethoxynaphth-2"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(2"-propoxynaphth-1"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(3"-propoxynaphth-1"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(4"-propoxynaphth-1"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(5"-propoxynaphth-1"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(6"-propoxynaphth-1"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-(7"-propoxynaphth-1"-yl)ethyl) **coformycin** aglycone,

SUMM 3-(2'-8"-propoxynaphth-1"-yl)ethyl) **coformycin** aglycone

SUMM 3-(2'-1"-propoxynaphth-2"-yl)ethyl) **coformycin** aglycone

SUMM 3-(2'-3"-propoxynaphth-2"-yl)ethyl) **coformycin** aglycone

SUMM 3-(2'-4"-propoxynaphth-2"-yl)ethyl) **coformycin** aglycone

SUMM 3-(2'-5"-propoxynaphth-2"-yl)ethyl) **coformycin** aglycone

SUMM 3-(2'-6"-propoxynaphth-2"-yl)ethyl) **coformycin** aglycone

SUMM 3-(2'-7"-propoxynaphth-2"-yl)ethyl) **coformycin** aglycone

SUMM 3-(2'-8"-propoxynaphth-2"-yl)ethyl) **coformycin** aglycone

SUMM 3-(3'-phenylpropyl) **coformycin** aglycone,

SUMM 3-(3'-(2"-methylphenyl)propyl) **coformycin** aglycone (compound  
1f),

SUMM 5-methyl-3-(3'-(2"-methylphenyl)propyl) **coformycin** aglycone  
(compound 1g),

SUMM 3-(3'-(2"-trifluoromethylphenyl)propyl) **coformycin** aglycone,

SUMM 3-(3'-(3"-methylthiophen-2"-yl)propyl) **coformycin** aglycone,

SUMM 3-(3'-2"-chlorophenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-3"-chlorophenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-2"-bromophenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-3"-bromophenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-2"-ethoxyphenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-3"-ethoxyphenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-4"-ethoxyphenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-2"-benzyloxyphenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-(3"-benzyloxyphenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-(4"-trifluoromethoxyphenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-(4"-butoxyphenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-(4"-isopropylphenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-(4"-propylphenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-(biphenyl-4"-yl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-(2",4"-dimethylphenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-(2",4",6"-trimethylphenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-(2"-hydroxyphenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(3'-(4"-hydroxyphenyl)propyl) **coformycin** aglycone,  
 SUMM 3-(5'-carboxypentyl) **coformycin** aglycone,  
 SUMM 3-(5'-(tetrazol-5"-yl)pentyl) **coformycin** aglycone,  
 SUMM 3-(5'-carbobenzyloxy-5'-carboxyhexyl) **coformycin** aglycone,  
 SUMM 3-(5'-carboxy-6'-phenylhexyl) **coformycin** aglycone (compound  
 1j),  
 SUMM 3-(5'-carboxy-6'-(2"-bromophenyl)hexyl) **coformycin** aglycone,  
 SUMM 3-(5'-carboxy-6'-(4"-bromophenyl)hexyl) **coformycin** aglycone,  
 SUMM 3-(5'-carbox-N-benzylamido-5'-carboxypentyl) **coformycin**  
 aglycone,  
 SUMM 3-(5'-carbox-N-(3"-bromobenzyl)amido-5'-carboxypentyl)  
**coformycin** aglycone,  
 SUMM 3-(5'-carbox-N-cyclohexylmethylamido-5'-carboxypentyl)  
**coformycin** aglycone,  
 SUMM 3-(5'-carbox-N-benzylamido-5'-carboxyhexyl) **coformycin** aglycone  
 (compound 1i),  
 SUMM 3-(5'-carbox-N-(2"-phenethyl)amido-5'-carboxyhexyl) **coformycin**  
 aglycone,  
 SUMM 3-(5'-carbox-N-cyclohexylamido-5'-carboxyhexyl) **coformycin**  
 aglycone,  
 SUMM 3-(5'-carbox-N-Cyclohexylmethylamido-5'-carboxyhexyl) **coformycin**  
 aglycone,  
 SUMM 3-(3'-(2"-fluoro-5"-carboxyphenyl)ethyl) **coformycin** aglycone,  
 SUMM 3-(2'-(2"-methoxy-5"-carboxyphenyl)ethyl) **coformycin** aglycone,  
 SUMM 3-(2'-(3"-carboxy-4"-methylphenyl)ethyl) **coformycin** aglycone,  
 SUMM 3-(2'-(3"-carboxy-4"-fluorophenyl)ethyl) **coformycin** aglycone,  
 SUMM 3-(2'-(3"-carboxy-5"-ethylphenyl)ethyl) **coformycin** aglycone,  
 SUMM 3-(2'-(3"-carboxybiphen-5"-yl)ethyl) **coformycin** aglycone,  
 SUMM 3-(2'-(3"-carboxy-6"-methylphenyl)ethyl) **coformycin** aglycone  
 (compound 1m),  
 SUMM 3-(2'-(6"-methyl-3"- (tetrazol-5'"-yl)phenyl)ethyl) **coformycin**  
 aglycone (compound 1n),  
 SUMM 3-(2'-(3"-carboxy-6"-ethylphenyl)ethyl) **coformycin** aglycone,  
 SUMM 3-(2'-(2"-carboxythiophen-4"-yl)ethyl) **coformycin** aglycone  
 (compound 1o),  
 SUMM 3-[2'-(2"-chloro-5"-carboxyphenyl)ethyl] **coformycin** aglycone,  
 SUMM 3-[2'-(2",3"-dichloro-5"-carboxyphenyl)ethyl] **coformycin**  
 aglycone,  
 SUMM 3-[2'-(2"-trifluoromethyl-5"-carboxyphenyl)ethyl] **coformycin**  
 aglycone,  
 SUMM 3-[2'-(3"-carboxy-5"-pentafluoroethylphenyl)ethyl] **coformycin**  
 aglycone,  
 SUMM 3-[2'-(3"-carboxy-6"-pentafluoroethylphenyl)ethyl] **coformycin**  
 aglycone,  
 SUMM 3-[2'-(2"-chloro-3"-carboxyphenyl)ethyl] **coformycin** aglycone,  
 SUMM 3-[2'-2"-fluoro-3"-carboxyphenyl)ethyl] **coformycin** aglycone,  
 SUMM 3-[2'-2"-carboxythiophen-4-yl)ethyl] **coformycin** aglycone,

SUMM 3-[2'-2"-carboxyfuran-4-yl)ethyl]coformycin aglycone,  
SUMM 3-[2'-3"-carboxy-5"-chloronaphthyl)ethyl]coformycin aglycone,  
SUMM 3-[2'-3"-carboxy-5"-bromonaphthyl)ethyl]coformycin aglycone,  
SUMM 3-[2'-3"-carboxy-5"-trifluoromethyl naphthyl)ethyl]coformycin  
aglycone,  
SUMM 3-[2'-(3"-carboxy-5"-methylnaphthyl)ethyl]coformycin aglycone,  
SUMM 3-[2'-(3"-carboxy-5"-fluoronaphthyl)ethyl]coformycin aglycone,  
SUMM 3-[2'-(3"-carboxy-6"-chloronaphthyl)ethyl]coformycin aglycone,  
SUMM 3-[2'-(3"-carboxy-6"-bromonaphthyl)ethyl]coformycin aglycone,  
SUMM 3-[2'-(3"-carboxy-6"-trifluoromethyl naphthyl)ethyl]coformycin  
aglycone,  
SUMM 3-[2'-(3"-carboxy-6"-methylnaphthyl)ethyl]coformycin aglycone,  
SUMM 3-[2'-(3"-carboxy-6"-fluoronaphthyl)ethyl]coformycin aglycone,  
SUMM 3-[2'-(3'-carboxy-2"-chloronaphthyl)ethyl]coformycin aglycone,  
SUMM 3-[2'-(3"-carboxy-2"-fluoronaphthyl)ethyl]coformycin aglycone,  
SUMM 3-(5'-benzyl-5'-carboxy-5'-carbobenzyloxy-pentyl)coformycin  
aglycone,  
SUMM 3-(5'-carboxy-5'-carbox-N-benzylamidopentyl)coformycin  
aglycone,  
SUMM 3-(5'-carboxy-5'-carbox-N-cyclohexylamidopentyl)coformycin  
aglycone,  
SUMM 3-(5'-carboxy-5'-carbox-N-hexylamidopentyl)coformycin  
aglycone,  
SUMM 3-(5'-carboxy-5'-carbox-N-(4"-chlorobenzyl)amidopentyl)-  
coformycin aglycone.  
SUMM (3'S)-3-(3',7'-dimethyloct-6'-enyl)coformycin aglycone  
(compound 1c),  
SUMM 3-(3'-(4"-propoxyphenyl)propyl)coformycin aglycone (compound  
1i),  
SUMM 3-(5'-carboxy-5'-carbobenzyloxy-pentyl coformycin aglycone  
(compound 1k),  
SUMM 3-(2'-(3"-carboxynaphthyl)ethyl)coformycin aglycone (compound  
1p),  
SUMM 3-(2'-(3"-bromo-5"-carboxyphenyl)ethyl coformycin aglycone  
(compound 1q),  
SUMM 3-(5'-carboxy-6'-(3"-bromophenyl)hexyl)coformycin aglycone  
(compound 1r).  
SUMM . . . below. The key transformation in this preparation, the coupling  
step, is shown below, as is the numbering system of the  
coformycin aglycone. ##STR3##  
SUMM For certain indications compounds which are dual inhibitors of both AMP  
deaminase and ADA may be advantageous. Such compounds may have  
a synergistic activity due to inhibition of both enzymes and therefore  
would exhibit. . . doses and lower percent inhibition of each enzyme.  
For example, inhibition of AMPDA increases adenosine concentration to a  
level where ADA becomes important in adenosine metabolism,  
thus inhibition of both enzymes is synergistic. Also complete inhibition  
or nearly complete inhibition of. . . either enzyme would not be  
necessary. Toxicities due to lack of functional enzyme have been  
reported for both AMPDA and ADA-deficient humans. Complete  
ADA deficiency results in severe combined immunodeficiency.  
Complete AMPDA deficiency is reported to result in mild muscle fatigue.  
Use of a compound which inhibits both AMPDA and ADA would give  
beneficial effects without complete inhibition of either enzyme and  
therefore the use of such compounds would not result. . .  
SUMM AMPDA inhibitors having low activity as ADA inhibitors may be  
particularly suited for treatment of chronic conditions.  
SUMM Selective AMP deaminase inhibitors or mixed AMP deaminase and  
ADA inhibitors will be useful in the treatment of infections,  
especially those caused by protozoa and worms. They will also be. . .  
SUMM . . . deaminase. Moreover, we have shown that many of these compounds  
are specific inhibitors of AMP deaminase and inhibit adenosine deaminase  
(ADA) much less strongly.  
DETD 3-(3'-carboethoxypropyl)coformycin aglycone, mp

109°-112° C.;

DETD 3-(3'-carbobenzyloxypropyl)**coformycin** aglycone, mp 116°-117° C.;

DETD 3-(4'-carbomethoxybutyl)**coformycin** aglycone, mp 136°-139° C.;

DETD 3-(5'-carboethoxypentyl)**coformycin** aglycone, mp 115°-118° C.;

DETD 3-(6'-carboethoxyhexyl)**coformycin** aglycone, mp 117°-118° C.;

DETD 3-(7'-carbomethoxyheptyl)**coformycin** aglycone, mp 131°-133° C.;

DETD 3-(5'-carboethoxy-6'-phenylhexyl)**coformycin** aglycone, mp 121°-124° C.;

DETD 3-(5'-carboethoxy-6'-(2"-bromophenyl)hexyl)**coformycin** aglycone, mp 122°-125° C.;

DETD 3-(5'-carboethoxy-6'-3"-bromophenyl)hexyl)**coformycin** aglycone, mp 125°-127° C.;

DETD 3-(5'-carboethoxy-6'-(4"-bromophenyl)hexyl)**coformycin** aglycone, mp 114°-116° C.;

DETD 3-(5',5'-dicarboethoxyhexyl)**coformycin** aglycone, mp 122°-125° C.;

DETD 3-(5',5'-dicarbobenzyloxyhexyl)**coformycin** aglycone, mp 113°-116° C.;

DETD 3-(5',5',5'-tricarbobenzyloxy-pentyl)**coformycin** aglycone as a deliquescent solid;

DETD 3-(2'-(2"-carboethoxycyclopropyl)ethyl)**coformycin** aglycone cyclopropane isomers, mp 80°-88° C.;

DETD 3-(4'-carbomethoxybenzyl)**coformycin** aglycone, mp 185°-186° C.;

DETD 3-(4'-carbomethoxymethylbenzyl)**coformycin** aglycone, mp 170°-171° C.;

DETD 3-(3'-carboethoxymethylbenzyl)**coformycin** aglycone, mp 119° C.;

DETD 3-(2'-(2"-carbomethoxyphenoxy ethyl)**coformycin** aglycone, mp 180°-181° C.;

DETD 3-(4'-carbomethoxyphenylethyl)**coformycin** aglycone, mp 188°-189° C.;

DETD 3-(2'-(2"-carbomethoxyphenylthio)ethyl)**coformycin** aglycone, mp 179°-180° C.;

DETD 3-(2'-(2"-carbomethoxy-6"-isopropylphenylthio)ethyl)**coformycin** aglycone, mp 154° C.;

DETD 3-(3'-(2"-carbomethoxyphenyl)propyl)**coformycin** aglycone, mp 144° C.;

DETD 3-(3'-(2"-carbomethoxynaphthyl)propyl)**coformycin** aglycone, mp 98°-100° C.;

DETD 3-(2'-(3"-carbomethoxynaphthyl)ethyl)**coformycin** aglycone, mp 238° C.;

DETD 3-(cis-2'-(carbomethoxyethyl)cyclohexylmethyl)**coformycin** aglycone, mp 135°-140° C.;

DETD 3-(3'-(3"-carbomethoxyphenyl)propyl)**coformycin** aglycone, mp 140°-145° C.;

DETD 3-(3'-carbomethoxyphenylmethyl)**coformycin** aglycone, mp 205°-207° C.;

DETD 3-(3'-(3"-carbomethoxy-6-methylphenyl)propyl)**coformycin** aglycone, mp 165°-168° C.;

DETD 3-(3'-(3-N-methylcarboxamido-6"-methylphenyl)propyl)**coformycin** aglycone, mp 205° C.;

DETD 3-(3'-(2"-carbomethoxy-5"-methylphenyl)propyl)**coformycin** aglycone, mp 165°-170° C.;

DETD 3-(3'-(2"-carbomethoxy-4"-methylphenyl)propyl)**coformycin** aglycone, mp 144° C.;

DETD 3-(3'-(2"-carbomethoxy-3"-fluorophenyl)propyl)**coformycin** aglycone, mp 131° C.;

DETD 3-(2'-(3"-carboethoxy-5"-ethylphenyl)ethyl)**coformycin**



aglycone, mp 141° C.;

DETD 3-(2'-(3"-bromo-5"-carboethoxyphenyl)ethyl)**coformycin**  
aglycone, mp 132° C.;

DETD 3-(2'-(3"-carboethoxybiphen-5"-yl)ethyl)**coformycin** aglycone,  
mp 160° C.;

DETD 3-(2'-(3"-carbomethoxy-6"-methylphenyl)ethyl)**coformycin**  
aglycone, mp 199°-201° C.;

DETD 3-(2'-(3"-carboethoxy-6"-methylphenyl)ethyl)**coformycin**  
aglycone, mp 145°-150° C.;

DETD 3-(2'-(3"-carbobenzyloxy-6"-methylphenyl)ethyl)**coformycin**  
aglycone, mp 80°-85° C.;

DETD 3-(2-(3"-carboethoxy-6"-t-butyldimethylsilyloxy-methylphenyl) ethyl)  
**coformycin** aglycone as a deliquescent solid and standard  
treatment of this compound with TBAF provided 3-(2'-(3"-carboethoxy-6"-  
hydroxymethylphenyl)ethyl)**coformycin** aglycone as a  
deliquescent solid;

DETD 3-(2'-(3"-carbomethoxy-6"-ethylphenyl)ethyl)**coformycin**  
aglycone, mp 159° C.;

DETD 3-(2'-(3"-carbomethoxy-6"-propylphenyl)ethyl)**coformycin**  
aglycone, mp 164° C.;

DETD 3-(2'-(3"-carboethoxy-4"-methylphenyl)ethyl)**coformycin**  
aglycone, mp 155°-156° C.;

DETD 3-(2'-(3"-carbomethoxyphenyl)ethyl)**coformycin** aglycone, mp  
143° C.;

DETD 3-(3'-(2"-methoxy-5"-carbomethoxyphenyl)propyl)**coformycin**  
aglycone, mp 164° C.;

DETD 3-(2'-(2"-methoxy-5"-carbomethoxyphenyl)ethyl)**coformycin**  
aglycone, mp 190°-195° C.;

DETD 3-(2'-(2"-fluoro-5"-carbomethoxyphenyl)ethyl **coformycin**  
aglycone, mp 203°-205° C.;

DETD 3-(2'-(3"-carbomethoxy-4"-fluorophenyl)ethyl **coformycin**  
aglycone, mp 179°-180° C.;

DETD 3-(2'-(3"-carbomethoxyphenoxy)ethyl)**coformycin** aglycone, mp  
168°-170° C.;

DETD 3-(3'-(2"-carbomethoxyfuran-5"-yl)propyl)**coformycin** aglycone,  
mp 120°-122° C.;

DETD 3-(2'-carboethoxyfuran-5'-ylmethyl)**coformycin** aglycone, mp  
130°-135° C.;

DETD 3-(2'-(2"-carbomethoxythiophen-4"-yl)ethyl)**coformycin**  
aglycone, mp 171° C.;

DETD 3-(3'-(2"-carbomethoxythiophen-3"-yl)propyl)**coformycin**  
aglycone, mp 187° C.;

DETD 3-(3'-(2"-carbomethoxy-3"-methyl-6"-isopropylphenyl)propyl)  
**coformycin** aglycone, mp 175°-180° C.;

DETD 3-(3'-(2"-carbomethoxy-6"-isopropylphenyl)propyl)**coformycin**  
aglycone, mp 168°-170° C.;

DETD 3-(5'-dimethyl phosphonyl)pentyl)**coformycin** aglycone, mp  
80°-81° C.;

DETD 3-(6'-dimethyl phosphonyl)hexyl)**coformycin** aglycone, mp  
93°-94° C.;

DETD 3-(5'-(dibenzyl phosphonyl)pentyl)**coformycin** aglycone, mp  
81°-82° C.;

DETD 3-(6'-(dibenzyl phosphonyl)hexyl)**coformycin** aglycone, mp  
71°-72° C.;

DETD 3-(2'-acetoxylethyl)**coformycin** aglycone, mp  
164°-165° C.;

DETD 3-(3'-acetoxypentyl)**coformycin** aglycone, mp  
103°-104° C.;

DETD 3-(4'-acetoxypentyl)**coformycin** aglycone, mp  
134°-135° C.;

DETD 3-(5'-acetoxypentyl)**coformycin** aglycone, mp  
93°-94° C.;

DETD 3-(6'-acetoxylhexyl)**coformycin** aglycone, mp  
107°-108° C.;

DETD 3-(4'-cyanobutyl)**coformycin** aglycone, mp 146°-149° C.;  
 DETD 3-(6'-cyanoheptyl)**coformycin** aglycone, mp 129°-132° C.;  
 DETD 3-(3'-butenyl)**coformycin** aglycone, mp 151°-152° C.;  
 DETD 3-(trans-3',7'-dimethyl-2',6'-octadienyl)**coformycin** aglycone, mp 156°-158° C.;  
 DETD (3'R)-3-(3',7'-dimethyloct-6'-enyl)**coformycin** aglycone, mp 167°-168° C.;  
 DETD (3'S)-3-(3',7'-dimethyloct-6'-enyl)**coformycin** aglycone, mp 164°-165° C.;  
 DETD (3'S)-3-(3',7'-dimethyloctyl)**coformycin** aglycone, mp 170°-171° C.;  
 DETD 3-(4'-methyl-3'-pentenyl)**coformycin** aglycone, mp 160°-161° C.;  
 DETD (1'S,2'S,5'S)-3-(6',6'-dimethyl[3,1,1]-bicyclohept-2'-methyl)**coformycin** aglycone, mp 207°-208° C.;  
 DETD (1'R,2"S,5"R)-3-(2'-(2"-isopropyl-5"-methylcyclohexyloxy)-ethyl)**coformycin** aglycone, mp 168°-169° C.;  
 DETD (1"S,2"R,5"S)-3-(2'-(2"-isopropyl-5"-methylcyclohexyloxy)-ethyl)**coformycin** aglycone, mp 168°-169° C.;  
 DETD 3-(2'-cyclohexylethyl)**coformycin** aglycone, mp 205°-206° C.;  
 DETD 3-(3'-cyclohexylpropyl)**coformycin** aglycone, mp 180°-181° C.;  
 DETD 3-(2'-cyclopentylethyl)**coformycin** aglycone, mp 205°-206° C.;  
 DETD 3-(naphth-2'-ylmethyl)**coformycin** aglycone, mp 190°-191° C.;  
 DETD 3-(2'-(naphth-2"-yl)ethyl)**coformycin** aglycone, mp 192°-193° C.;  
 DETD 3-(2'-phenylethyl)**coformycin** aglycone, mp 146°-147° C.;  
 DETD 3-(2'-(2"-methylphenyl)ethyl)**coformycin** aglycone, mp 180°-185° C.;  
 DETD 3-(3'-phenylpropyl)**coformycin** aglycone, mp 157°-158° C.;  
 DETD 3-(3'-(2",3",4",5"-tetrafluorophenyl)propyl)**coformycin** aglycone, mp 188°-189° C.;  
 DETD 3-(3'-phenyl-2'-propenyl)**coformycin** aglycone, mp 168°-169° C.;  
 DETD 3-(3'-(2"-methylphenyl)propyl)**coformycin** aglycone, mp 193°-195° C.;  
 DETD 3'-(2"-trifluoromethylphenyl)propyl)**coformycin** aglycone, mp 188°-192° C.;  
 DETD 3'-(3"-methylthiophen-2"-yl)propyl)**coformycin** aglycone, mp 185°-190° C.;  
 DETD 3-(3'-(2"-chlorophenyl)propyl)**coformycin** aglycone, mp 181°-182° C.;  
 DETD 3-(3'-3"-chlorophenyl)propyl)**coformycin** aglycone, mp 171°-172° C.;  
 DETD 3-(3'-4"-chlorophenyl)propyl)**coformycin** aglycone, mp 157°-158° C.;  
 DETD 3-(3'-2"-bromophenyl)propyl)**coformycin** aglycone, mp 186°-187° C.;  
 DETD 3-(3'-3"-bromophenyl)propyl)**coformycin** aglycone, mp 165°-166° C.;  
 DETD 3-(3'-4"-bromophenyl)propyl)**coformycin** aglycone, mp 147°-148° C.;  
 DETD 3-(3'-2"-ethoxyphenyl)propyl)**coformycin** aglycone, mp 168°-169° C.;  
 DETD 3-(3'-3"-ethoxyphenyl)propyl)**coformycin** aglycone, mp 136°-137° C.;

DETD 3-(3'-(4"-ethoxyphenyl)propyl)**coformycin** aglycone, mp 117°-118° C.;

DETD 3-(3'-(2"-benzyloxyphenyl)propyl)**coformycin** aglycone, mp 129°-130° C.;

DETD 3-(3'-(3"-benzyloxyphenyl)propyl)**coformycin** aglycone, mp 123°-124° C.;

DETD 3-(3'-(4"-benzyloxyphenyl)propyl)**coformycin** aglycone, mp 154°-155° C.;

DETD 3-(3'-(4"-methoxyphenyl)propyl)**coformycin** aglycone, mp 165°-166° C.;

DETD 3-(3'-(4"-trifluoromethoxyphenyl)propyl)**coformycin** aglycone, mp 123°-124° C.;

DETD 3-(3'-(4"-propoxyphenyl)propyl)**coformycin** aglycone, mp 134°-135° C.;

DETD 3-(3'-(4"-butoxyphenyl)propyl)**coformycin** aglycone, mp 135°-136° C.;

DETD 3-(3'-(4"-isopropylphenyl)propyl)**coformycin** aglycone, mp 161°-162° C.;

DETD 3-(3'-(4"-propylphenyl)propyl)**coformycin** aglycone, mp 139°-140° C.;

DETD 3-(3'-(biphenyl-4"-yl)propyl)**coformycin** aglycone, mp 174°-175° C.;

DETD 3-(3'-(2", 4"-dimethylphenyl)propyl)**coformycin** aglycone, mp 167° C.;

DETD 3-(3'-(2", 5"-dimethylphenyl)propyl)**coformycin** aglycone, mp 174° C.;

DETD 3-(3'-(2", 4", 6"-trimethylphenyl)propyl)**coformycin** aglycone, mp 181° C.;

DETD 3-(2'-phenylbutyl)**coformycin** aglycone, mp 161°-162° C.; and

DETD 3-(6'-(2"-bromophenyl)hexyl)**coformycin** aglycone, mp 136°-137° C.;

DETD Preparation of 3-(3'-(Hydroxyphenyl)propyl)**coformycin** Aglycones.

DETD The 3-(3'-(benzyloxyphenyl)propyl)**coformycin** aglycone was hydrogenated using previously described conditions to provide the title compound.

DETD 3-(3'-(2"-hydroxyphenyl)propyl)**coformycin** aglycone, mp 140°-141° C.;

DETD 3-(3'-(3"-hydroxyphenyl)propyl)**coformycin** aglycone, mp 144°-145° C.; and

DETD 3-(3'-(4"-hydroxyphenyl)propyl)**coformycin** aglycone, mp 123°-124° C.

DETD Preparation of 5-Methyl-3-(3'-(2"-methylphenyl)propyl)-**coformycin** aglycone.

DETD Preparation of 7-Methyl-3-(3'-phenylpropyl)**coformycin** aglycones.

DETD Preparation of 3-Cycloheptyl **Coformycin** Aglycone.

DETD A mixture of 1 mmol of a 3-substituted **coformycin** aglycone and 3 mmol of thioacetic acid in 10 mL of DMF was stirred at rt for 16 h. Chromatography.

DETD 3-(5-carboxypentyl)**coformycin** aglycone sodium salt, mp 250° C. (dec);

DETD 3-(6'-carboxyhexyl)**coformycin** aglycone, mp 165°-168° C.;

DETD 3-(7'-carboxyheptyl)**coformycin** aglycone, mp 166°-166° C.;

DETD 3-(3'-carboxypropoxymethyl)**coformycin** aglycone sodium salt as a deliquescent solid;

DETD 3-(5'-carbobenzyloxy-5'-carboxyhexyl)**coformycin** aglycone sodium salt, and in this case, dioxane in a volume equivalent to that of sodium hydroxide was added to.

DETD 3-(2'-(2"-carboxycyclopropyl)ethyl)**coformycin** aglycone sodium salt as a deliquescent solid,

DETD 3-(2'-(o-carboxyphenoxy)ethyl)**coformycin** aglycone sodium salt as a deliquescent solid,  
 DETD 3-(p-carboxyphenylethyl)**coformycin** aglycone sodium salt as a deliquescent solid,  
 DETD 3-(p-carboxymethylbenzyl)**coformycin** aglycone sodium salt as a deliquescent solid,  
 DETD 3-(2'-(o-carboxyphenylthio)ethyl)**coformycin** aglycone sodium salt as a deliquescent solid,  
 DETD 3-(2'-(m-carboxyphenoxy)ethyl)**coformycin** aglycone sodium salt as a deliquescent solid,  
 DETD 3-(3'-(3"-carboxy-6"-methylphenyl)propyl)**coformycin** aglycone sodium salt as a deliquescent solid,  
 DETD 3-(3'-(o-carboxyphenyl)propyl)**coformycin** aglycone sodium salt as a deliquescent solid,  
 DETD 3-(3'-(m-carboxyphenyl)propyl)**coformycin** aglycone sodium salt as a deliquescent solid and  
 DETD 3-(3'-(mercaptoacetoxyl)propyl)**coformycin** aglycone sodium salt as a deliquescent solid.  
 DETD 3-(5'-carboxy-6'-phenylhexyl)**coformycin** aglycone, prepared as described only an equal volume of dioxane was added and the mixture was heated for 16 h. . . .  
 DETD 3-(5'-carboxy-6'-(2"-bromophenyl)hexyl)**coformycin** aglycone, mp 111° C.;  
 DETD 3-(5'-carboxy-6'-3"-bromophenyl)hexyl)**coformycin** aglycone, mp 98° C.;  
 DETD 3-(5'-carboxy-6'-4"-bromophenyl)hexyl)**coformycin** aglycone, mp 116° C.;  
 DETD 3-(5',5'-dicarboxypentyl)**coformycin** aglycone, prepared as described from 3-(5',5',5'-tricarbobenzyloxy-pentyl)**coformycin** aglycone only an equal volume of dioxane and 2 mmol of NaOH were added and the product was isolated by. . . .  
 DETD 3-(5'-carboxy-5'-carbobenzyloxy-pentyl)**coformycin** aglycone, prepared as described from 3-(5',5',5'-tricarbobenzyloxy-pentyl)**coformycin** aglycone only an equal volume of dioxane and 2 mmol of NaOH were added and the product was isolated by. . . .  
 DETD 3-(3'-(2'-carboxy-5"-methylphenyl)propyl)**coformycin** aglycone, mp 122°-125° C.;  
 DETD 3-(3'-(2'-carboxyphenylmethyl)**coformycin** aglycone, mp 205°-207° C.;  
 DETD 3-(3'-(2'-carboxyfuran-5"-yl)propyl)**coformycin** aglycone, 190° C. (dec);  
 DETD 3-(2'-carboxyfuran-5"-ylmethyl)**coformycin** aglycone, mp 240° C. (dec);  
 DETD 3-(3'-(2"-carboxy-6"-isopropylphenyl)propyl)**coformycin** aglycone, mp 210° C. (dec);  
 DETD 3-(3'-(2'-methoxy-5"-carboxyphenyl)propyl)**coformycin** aglycone, mp 225° C.;  
 DETD 3-(3'-(2'-fluoro-5"-carboxyphenyl)ethyl)**coformycin** aglycone, mp 230°-240° C.;  
 DETD 3-(2'-(2"-methoxy-5"-carboxyphenyl)ethyl)**coformycin** aglycone, mp 180°-190° C. (dec);  
 DETD 3-(2'-(3"-carboxy-4"-methylphenyl)ethyl)**coformycin** aglycone as a deliquescent solid;  
 DETD 3-(2'-(3"-carboxy-4"-fluorophenyl)ethyl)**coformycin** aglycone, mp 220°-230° C. (dec);  
 DETD 3-(2'-(3"-carboxy-5"-ethylphenyl)ethyl)**coformycin** aglycone, mp 130° C. (dec);  
 DETD 3-(2'-(3"-carboxybiphen-5"-yl)ethyl)**coformycin** aglycone, mp 220° C. (dec);  
 DETD 3-(2'-(3"-bromo-5"-carboxyphenyl)ethyl)**coformycin** aglycone, mp 226° C.;  
 DETD 3-(2'-(3"-carboxy-6"-methylphenyl)ethyl)**coformycin** aglycone, mp 140°-150° C.;  
 DETD 3-(2'-(3"-carboxy-6"-ethylphenyl)ethyl)**coformycin** aglycone, mp

215° C.;

DETD 3-(2'-(3"-carboxy-6"-propylphenyl)ethyl)**coformycin** aglycone, mp 250° C.;

DETD 3-(2'-(3"-carboxy-6"-hydroxymethylphenyl)ethyl)**coformycin** aglycone, mp 140°-150° C.;

DETD 3-(2'-(3"-carboxyphenyl)ethyl)**coformycin** aglycone, mp 210° C.;

DETD 3-(3'-(2"-carboxy-3"-fluorophenyl)propyl)**coformycin** aglycone, mp 205° C.;

DETD 3-(3'-(2"-carboxy-4"-methylphenyl)propyl)**coformycin** aglycone, mp 204° C.;

DETD 3-(3'-(2"-carboxymethylbenzyl)**coformycin** aglycone, mp 207° C.;

DETD 3-(3'-(2"-carboxynaphthyl)propyl)**coformycin** aglycone, mp 200°-210° C.;

DETD 3-(2'-(3"-carboxynaphthyl)ethyl)**coformycin** aglycone, mp 190°-235° C. (dec);

DETD 3-(3'-(2"-carboxythiophen-3"-yl)propyl)**coformycin** aglycone, mp 210° C. (dec);

DETD 3-(2'-(2"-carboxythiophen-4"-yl)ethyl)**coformycin** aglycone, mp 230° C. (dec);

DETD 3-(2'-(2"-carboxythiophen-5"-yl)ethyl)**coformycin** aglycone as a deliquescent solid and

DETD A mixture of 1 mmol of 3-(3'-(3"-carboxypropyl)**coformycin** aglycone and 10 mg of 10% Pd/C in 4 mL of methanol was subjected to hydrogenation. After filtration and removal of the solvent, 3-(3'-(3"-carboxypropyl)**coformycin** aglycone was obtained. This product, 2 mmol glycine ethyl ester hydrochloride, 2 mmol triethylamine, 2 mmol dicyclohexylcarbodiimide and 2 mmol.

DETD Preparation Of 3-(5'-(3"-carbox-N-substituted-amido-5'-carboxyhexyl)**coformycin** Aglycones.

DETD A mixture of 1 mmol of 3-(5'-(3"-carbox-N-benzylamido-5'-carboxyhexyl)**coformycin** aglycone, 1.5 mmol of an amine, 1.5 mmol of diphenylphosphoryl azide and 3 mmol of triethylamine in 10 mL of DMF.

DETD 3-(5'-(3"-carbox-N-benzylamido-5'-carboxyhexyl)**coformycin** aglycone, mp 175° C.;

DETD 3-(5'-(3"-carbox-N-(4"-chlorobenzyl)amido-5'-carboxyhexyl)**coformycin** aglycone, mp 111° C.;

DETD 3-(5'-(3"-carbox-N-(2"-phenethyl)amido-5'-carboxyhexyl)**coformycin** aglycone, mp 93° C.;

DETD 3-(5'-(3"-carbox-N-cyclohexylamido-5'-carboxyhexyl)**coformycin** aglycone, mp 199°-203° C.; and

DETD 3-(5'-(3"-carbox-N-cyclohexylmethylamido-5'-carboxyhexyl)**coformycin** aglycone, mp 116° C.

DETD Preparation of 3-(5'-(3"-carbox-N-amido-5'-carboxyhexyl)**coformycin** Aglycone.

DETD The compound 3-(5'-(3"-carbox-N-phenylamido-5'-carboxyhexyl)**coformycin** aglycone, prepared as above was subjected to hydrogenation by the previously described method to provide the title compound: mp 170°.

DETD Preparation of 3-(5'-(3"-carbox-N-(Tetrazol-5"-yl)pentyl)**coformycin** aglycone dicyclohexylammonium salt.

DETD 6,7-Dihydroimidazo[4,5-d][1,3]diazepin-8(3H)-one and 5-(5'-bromopentyl)-2-trimethylsilylethoxy-methyltetrazole were subjected to the general alkylation and reduction sequence to provide 3-(5'-(3"-carbox-N-(2"-trimethylsilylethoxy-methyl)tetrazol-5"-yl)pentyl)**coformycin** aglycone as a deliquescent solid.

DETD 3-(2'-(6"-methyl-3-(tetrazol-5"-yl)phenyl)ethyl)**coformycin** aglycone: mp 190° C. (dec).

DETD Preparation of 3-(6'-(Methyl phosphonoxy)hexyl)**coformycin** Aglycone.

DETD A solution of 1 mmol of 3-[6'-(dimethyl phosphonyl)hexyl]**coformycin** aglycone and 20 mmol lithium methoxide in 10 mL of

methanol was stirred for 72 h at 50° C. The. . .

DETD Preparation of 3-(5'-Phosphonoxypentyl)**coformycin** Aglycone.

DETD A suspension of 1 mmol of 3-[5'-(dibenzyl phosphonyl)pentyl]**coformycin** aglycone and 50 mg of 10% Pd/C in 10 mL of 1:1 water-methanol was hydrogenated. The mixture was filtered through Celite, . . .

DETD 3-(6'-phosphonoxyhexyl)**coformycin** aglycone, mp 210° C. (dec);

DETD and 3-(5',5'-dicarboxyhexyl)**coformycin** aglycone dicyclohexyl ammonium salt, prepared in the same manner only dicyclohexylamine was included during hydrogenation, mp 155° C. (dec).

DETD General Procedure for Acetate Methanolysis to a 3-(Hydroxyalkyl)**coformycin** Aglycone.

DETD A solution of 1 mmol of 3-(acetoxymethyl)**coformycin** aglycone and 5 mL of a 0.5M solution of sodium methoxide in methanol was stirred for 0.5 hours. Amberlite CG-50. . .

DETD 3-(2'-hydroxyethyl)**coformycin** aglycone, mp 220°-221° C.;

DETD 3-(3'-hydroxypropyl)**coformycin** aglycone, mp 210°-211° C.;

DETD 3-(4'-hydroxybutyl)**coformycin** aglycone, mp 176°-177° C.;

DETD 3-(5'-hydroxypentyl)**coformycin** aglycone, mp 135°-136° C.; and

DETD 3-(6'-hydroxyhexyl)**coformycin** aglycone, mp 138°-139° C.

DETD Preparation of 3-(5'-Carboxamidopentyl)**coformycin** Aglycone.

DETD A solution of 3-(5'-carboethoxypentyl)**coformycin** aglycone in 4 mL of a 15% NH<sub>3</sub> in methanol solution was heated in a sealed reaction vessel at 100° . . .

DETD (3'S)-3-(3',7'-dimethyloct-6'-enyl)**coformycin** aglycone (compound 1c),

DETD (1'S,2'S,5'S)-3-(6',6'-dimethyl[3,1,1]-bicyclohept-2'-methyl)**coformycin** aglycone (compound 1e),

DETD 3-(3'-(2"-methylphenyl)propyl)**coformycin** aglycone (compound 1f),

DETD 5-methyl-3-(3'-(2"-methylphenyl)propyl)**coformycin** aglycone (compound 1g),

DETD 3-(3'-(4"-propoxyphenyl)propyl)**coformycin** aglycone (compound 1i),

DETD 3-(5'-carboxy-6'-phenylhexyl)**coformycin** aglycone (compound 1j),

DETD 3-(5'-carboxy-5'-carbobenzyloxypentyl)**coformycin** aglycone (compound 1k),

DETD 3-(5'-carboxy-N-benzylamido-5'-carboxyhexyl)**coformycin** aglycone (compound 1l),

DETD 3-(2'-(3"-carboxy-6"-methylphenyl)ethyl)**coformycin** aglycone (compound 1m),

DETD 3-(2'-(6"-methyl-3"-(tetrazol-5"-yl)phenyl)ethyl)**coformycin** aglycone (compound 1n),

DETD 3-(2'-(2"-carboxythiophen-4"-yl)ethyl)**coformycin** aglycone (compound 1o),

DETD 3-(2'-(3"-carboxynaphthyl)ethyl)**coformycin** aglycone (compound 1p),

DETD 3-(2'-(3"-bromo-5"-carboxyphenyl)ethyl)**coformycin** aglycone (compound 1q) and

DETD 3-(5'-carboxy-6'-(3"-bromophenyl)hexyl)**coformycin** aglycone (compound 1r).

DETD Inhibition of adenosine deaminase (ADA) from calf intestinal mucosa was determined spectrophotometrically at pH 7.0 using one of the following two assays:

DETD (1) Direct Assay: The reaction system mixture contained inhibitor, .about.0.001 units ADA, and 40 mM potassium phosphate in 1 mL and at 37° C. The concentration of the substrate adenosine was

varied from 20 to 100  $\mu$ M. The reaction was initiated by addition of **ADA** and monitored continuously at 265 nm for 15 minutes as the decrease in absorbance reflects conversion of adenosine to inosine.

DETD (2) Coupled Assay Based Upon the Following Reaction Scheme: ##STR53##  
The reaction mixture contained 100  $\mu$ M adenosine, .about.0.001 U **ADA**, 2.5 mM a-ketoglutarate (aKG), 250  $\mu$ M NADH, 400  $\mu$ M ADP, .about.10 U glutamate dehydrogenase (GDH), and 50 mM potassium phosphate.

DETD The following table gives the inhibition constants for AMPDA and **ADA** of representative compounds of the present invention. The selectivity ratio was determined as: selectivity ratio=[**ADA** Ki/Km]/[AMPDA Ki/Km].

DETD

Compound	AMPDA Ki*	<b>ADA</b> Ki*	Selectivity Ratio**
----------	-----------	----------------	---------------------

1a	10	0.35	0.60
1b	36	12	6
1c	1.1	1.9	29
1d	8.0	7.9	17
1e	1.7	>160	>1.6K
1f	2.1	0.042.	.

DETD . . . values obtained for representative compounds of the present invention. This inhibition was completely reversed in the presence of adenosine deaminase (**ADA**), demonstrating inhibition was mediated by increased adenosine levels.

=>